UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/057,275	10/25/2001	Roger Coleman	PF-0027-1 CON	3250

22428 7590 09/20/2004

FOLEY AND LARDNER
SUITE 500
3000 K STREET NW
WASHINGTON, DC 20007

EXAMINER	
SWITZER, JULIET CAROLINE	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 09/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/057,275	COLEMAN ET AL.	
	Examiner	Art Unit	
	Juliet C. Switzer	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18,20,23 and 60-66* is/are pending in the application.

4a) Of the above claim(s) *1,2,11,14-18,20 and 23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-10,12,13 and 60-66* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This action is written in response to applicant's correspondence submitted 6/14/04. Claims 1-18, 20, 23, and 60-66 are pending. Claims 1-2, 11, 14-18, 20, and 23 are withdrawn from prosecution as being drawn to non-elected inventions. In the paper filed 6/14/04, claims 3, 4, 5, 12, and 13 were amended and claims 62-66 have been added. Claims 3-10, 12-13, and 60-66 are under examination herein. Applicant's amendments and arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections not reiterated in this action have been withdrawn. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Priority

2. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application); the disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994). In the instant case, the amendments to the claims introduce the phrase "having at least 90% sequence identity to the amino acid sequence of SEQ ID NO: 4" which is not supported by written description in the prior application (see instant claims 3 and 62). This amendment has support in the instant application in the claims as originally filed in the instant application. Likewise, for the parent application does not provide support for the

limitations of the claims that are addressed in the new matter rejection herein. Therefore, since claims 3, 3, 6, 7, 8, 9, 10, 60, 61, 62, 63, 64, and 65 contain language that does no have support in the parent application, priority is not granted to the parent application for these claims.

3. Applicant is required to (A) file a new oath or declaration along with the surcharge set forth in 37 CFR 1.16(e) and (B) redesignate the current application as a continuation-in-part (see MPEP 201.06(c)(III)).

Dependence from Non-elected Claims

4. It is noted that claims 9-10 both depend from non-elected claim 1. Prior to allowance of claims 9-10 they will be required to be amended so that they do not depend from non-elected claims.

Claim Rejections - 35 USC § 112- New Matter

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 9-10, 60, 61, and 65 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. In re Rasmussen , 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)."

(A) In claims 9, 10, and 65, the limitations of "has an insertion or deletion of 1-5 amino acids as compared with SEQ ID NO: 4" and/or "has one or more amino acid substitutions as compared with SEQ ID NO: 4, and has the amino acid sequence of SEQ ID NO: 4 at amino acids 1, 4, 6, 7, 10, etc..." in claim 1 (from which claims 9-10 depend) and in claim 65 appear to represent new matter.

In the remarks filed with the amendment first entering these limitations (in the preliminary amendment), applicant points to page 8, lines 1-2 as stating "The DNAs which encode PANEC-1 and PANEC-2 may also include allelic or recombinant variants and mutants thereof (p. 11 of the paper)." It is noted that this statement is not located on page 8 of the specification, but instead on page 7, lines 19-20. Nonetheless, it is agreed that this statement generically provides support for the language "allelic or recombinant variant" from a new matter perspective. However, the specific limitations repeated in this rejection are not adequately supported by this recitation as this recitation does not discuss the length of any possible deletion, nor does this recitation discuss any particular amino acids that are necessary to be retained in a variant of SEQ ID NO: 4.

Applicant further points to the specification at figures 3A, 3B, and 3C as providing support for the various limitations in the amounts and types of insertions, deletions and substitutions. Applicant states that Figure 3A, 3B, and 3C compare PANEC-2 (SEQ ID NO: 4) to its three closest prior art molecules at the time of the invention, namely MIP-1a, MIP-1b, and RANTES. Figure 3 also compares SEQ ID NO: 4 (referred to therein as 226252) to MCP-1, MCP-2, MCP-3, and instant SEQ ID NO: 2, referred to in Figure 3 as 223187. The remarks state that the numbers utilized in the instant claims are "mathematical calculations of sequence

selections" based on figures 3A, 3B, and 3C. However, there does not appear to be basis for these calculations in the specification.

Applicant points to page 7, lines 6-7 as supporting the language "has an insertion or deletion of 1-5 amino acids as compared with SEQ ID NO: 2." It is noted that the sequence recited in the pending claims is SEQ ID NO: 4, not SEQ ID NO: 2. Nonetheless, this portion of the specification defines the terms "oligonucleotide" and polynucleotide "fragment", "portion" or "segment" and does not appear to discuss deletions of 1-5 amino acids in polypeptides. The previous page discusses amino acid insertions, deletions and substitutions, and states that "Guidance in determining which amino acid residues may be replaced, added, or deleted without abolishing activities of interest, such a cell adhesion and chemotaxis, may be found by comparing the sequence of the particular PANEC with that of homologous cytokines and minimizing the number of amino acid sequence changes made in regions of high homology (p. 6, fifth paragraph)." This language does not discuss a number of amino acids that may be inserted or deleted in this "minimizing" process, and thus, the claims are rejected as containing new matter over this recitation.

Applicant points to this same section in the fifth paragraph of page 6 as support for the amendments which recite the long listing of amino acids that must be common to the variants, suggesting in the remarks that "by counting the number of amino acid changes between PANEC-2 with respect to all three of the prior art MCPs disclosed in the specification, further stating that the specification provides guidance for and supports identification of specific amino acid residues of PANEC-2 which should be retained in a variant, "i.e., wherein 2 of the three MIPs and/or RANTES ("homologous cytokines") have the same amino acid at a specific location...as

PANEC-2, and by allowing only sequence variation at residues where PANEC-2 differs from at least 2 of the three MIPs and/or RANTES." This is not persuasive.

The generic guidance in the specification does not make readily apparent the specific guidance given in the remarks. The generic guidance repeatedly cited by applicant is vague at best, referring to "homologous cytokines" but not stating what degree of homology is required, and also guiding one to "minimize" the number of amino acid changes in regions of "high homology," but never qualifying these relative phraseologies with actual limitations. The guidance provided in applicant's remarks is quite detailed, the details of which do not appear to be based on the specification but on criteria that are not recited in the specification. Furthermore, applicant's own guidance on page 12 of the response conflicts, referring to counting the amino acid changes between the MCPs and SEQ ID NO: 4 in the beginning of the paragraph, and then at the latter half of the paragraph referring to comparisons of PANEC-2 with the MIPs and/or RANTES. Nonetheless, the specification does not give any guidance as to why one would preferentially compare SEQ ID NO: 4 to any of the sequences given in figure 3, and indeed, in Figure 3, SEQ ID NO: 4 is compared to all of these sequences, or so it appears, based on the shading that overlaps with all of the sequences at some positions (for example at amino acid numbered 61 of the "majority").

Most of applicant's selections of the amino acid residues in claim 1 appear to follow the "two of three" rule set forth in the remarks with regard to MIPs and/or RANTES. It does not apply to all of the residues recited in claim 1, however, for example, required residue 50 in the PANEC-2 molecule is a glutamic acid (E), yet none of the other cytokines appear to share this residue at the aligned position (see Figure 3B). Furthermore, the "two of three rule," as noted,

does not appear to be supported in the specification. It is not clear why one would choose, based on the guidance in the specification to "minimize" differences with these three sequences as opposed to the other four sequences given in Figure 3. Instant SEQ ID NO: 4 is compared to seven total sequences in Figure 3, and there is no clear guidance in the specification as to when describing a "variant" of SEQ ID NO: 4 one would look only to three of these seven sequences for guidance. For example, at position 47 of instant SEQ ID NO: 4 shares a serine residue with the three MCP molecules and with SEQ ID NO: 2. However, this is not an amino acid position recited in the "required" amino acids of claims 1 and 12. Given the general guidance in the specification, the instant amendments reciting particular numbers of insertions or deletions and reciting specific amino acid numbers are not supported.

Because no specific basis for these limitations was identified in the specification, nor did a review of the specification by the examiner find any basis for the limitations, the claims are rejected as incorporating new matter.

(B) Further, turning to claims 60 and 61, in particular, in these claims the negative limitations "is non-genomic" and "without introns" appear to be new matter. In applicant's remarks at page 14, applicant suggests that these limitations are supported as "the negative" of the definition in the specification on page 10, lines 2-3. This portion of the specification reads "The hybridization probes of the subject invention may be derived from the nucleotide sequences of the SEQ ID NO:1 or SEQ ID NO:3 from genomic sequences including promoters, enhancer elements and introns of the respective naturally occurring panecs (specification p. 10, lines 1-3)," thus clearly setting forth that applicant intends for the hybridization probes of their invention to

encompass genomic DNA, specifically reciting introns as included within the genus of hybridization probes. As noted by MPEP 2173.05(i),

"Any negative limitation or exclusionary proviso must have basis in the original disclosure. See Ex parte Grasselli , 231 USPQ 393 (Bd. App. 1983) aff'd mem., 738 F.2d 453 (Fed. Cir. 1984). The mere absence of a positive recitation is not basis for an exclusion...Any claim containing a negative limitation which does not have basis in the original disclosure should be rejected under 35 U.S.C. 112, first paragraph as failing to comply with the written description requirement."

In this case, there is not absence of a positive recitation, but instead, there is presence of a positive recitation, and no suggestion within the specification of the negative limitations. Since no basis for the negative limitations has been identified, the claims are rejected as incorporating new matter.

Claim Rejections - 35 USC § 101/112 1st, Lack of Utility

6. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

7. Claims 1-10, 12, 13, 60, 61, and 62-65 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

The claims are drawn to isolated polynucleotides encoding instant SEQ ID NO: 4 or a variety of variants and/or fragments of instant SEQ ID NO: 4 which have "chemokine activity" or which are "immunogenically active fragments." The claims further recite constructs

comprising these nucleic acids, including vectors and host cells/organisms, as well as methods for producing polypeptides which utilize these constructs.

The specification teaches that instant SEQ ID NO: 3 encodes instant SEQ ID NO: 4, a polypeptide referred to in the specification as PANEC-2. The specification teaches that PANEC-2 is a human pancreatic protein that is a member of the C-C chemokine family, based on the fact that the molecule was isolated from a library obtained from human pancreatic tissue and based on homology of SEQ ID NO: 4 to other C-C chemokines.

The specification asserts that PANEC-2 is specifically expressed in pancreas, and because of this PANEC-2 nucleic acids are useful in assays based on chemokine production in cases of inflammation or disease affecting the pancreas (p. 8). While asserted utility is specific, it is not substantial. It is not substantial because further experimentation would be required to reasonably confirm that in fact a real world utility exists wherein these molecules can be used in diagnostics.

Chemokines are chemoattractant cytokines. In a 1994 review of chemokines, Schall *et al.* teach that "Although the properties of these molecules have only recently begun to be elucidated, the bulk of the evidence to date suggests that the chemokines function as regulators of inflammatory and immunoregulatory processes, particularly through their leukocyte chemoattractant effects (p. 4, third paragraph, as cited in the IDS)." A "leukocyte" is a white blood cell, and includes among its members monocytes, neutrophils, basophils, eosinophils, and lymphocytes, each of which function differently within the body's immune system. Furthermore, Schall *et al.* provide a table which summarizes different sources and targets for the known C-C type chemokines (Table V). Some of these, for example MCP-1, can be isolated

from many tissues, while others can be isolate from only T cells (for example I-309). Likewise, with regard to targets, some of the C-C type chemokines target a wide variety of cells, for example MIP-1α targets a variety of leukocytes as well as stem cells, osteoclasts, and hypothalamus. And for some the target is yet unknown, such as the murine C-C chemokine C10. Furthermore, Schall *et al.* teach that even chemokines with a great deal of structural homology (70%) demonstrate distinct specificities for their cellular targets (p. 16, first full paragraph), and that attempts to even elucidate the targets of chemokines contain "pitfalls of interpretation (p. 23, second paragraph)." The pancreas is a complex organ with many cell types- the specification does not provide any information as to what type of cells produce or are targeted by PANEC-2. Thus, in the instant case, while applicant may have identified a C-C type chemokine, this designation does not speak specifically to the functioning of the molecule with regard to target, and further experimentation (which is unpredictable) would be required to determine such a target. Without knowledge of such a target, it would be difficult to utilize the instant molecule in diagnostics or prognostics because it is unknown what the presence of the molecule would indicate or suggest.

Furthermore, the instant specification asserts that the PANEC-2 molecule is "specifically" expressed in pancreas and can therefore be used in assays to detect diseases or inflammation of the pancreas. However, the specification does not provide any evidence of this specific expression, only teaching that the molecule was isolated from a human pancreatic cDNA library, but never assaying additional tissue types to determine the specificity of expression. Accordingly, the assertion that PANEC-2 is "specifically" expressed in the pancreas is not substantial. All that can be concluded based upon the specification as filed is that PANEC-2 is

expressed in pancreas, not that such expression is specific to pancreas. Indeed, the post-filing date art suggests that the PANEC-2 molecule (SEQ ID NO: 4) is expressed in a wide variety of tissues, including lymph nodes, appendix, heart, small intestine, colon, and spleen (Nagira *et al.*, 1997, figure 3). This reference supports the position that at the time the invention was made further experimentation would have been necessary to even reasonably confirm the expression specificity of the instant molecule.

The specification does not elucidate or demonstrate any particular target for the instantly disclosed chemokine, but instead teaches that excessive expression of PANEC-2 "can" lead to activation of monocytes, macrophages, basophils, eosinophils, T lymphocytes, and/or other cells which respond to chemokines. The language of the specification appears to be prophetic, and suggests that PANEC-2 may activate any one of these or some other undisclosed molecule, but it is equally suggestive that it may not activate any one of these. This is not a definitive assertion of functionality or utility. It is also noted that chemokines are particularly discussed in the specification at several citations regarding their broad activities. For example, on pages 2-3, various chemokines are described with varying activities discussed. Particular attention is drawn to page 3, line 9, wherein it is stated that chemokine activities demonstrate a high degree of target cell specificity. This statement is significant in that the subject matter of the instant claims is "not" characterized as target cell specificity other than the generic pancreas location thereof. Numerous activities are carried out by the pancreas, including numerous non-chemokine activities, and thus this pancreas specificity is generic in nature, especially since the chemokines encoded by the instantly claimed nucleic acids have no asserted correlation to any particular disease or illness, but rather only speculated as being involved in a long list of diseases or

illnesses. Thus, the asserted utility of the claimed PANEC-2 encoding nucleic acids as a tool in diagnostics is not substantial because the specification does not teach or suggest the "inflammatory or disease" affecting the pancreas that can be identified using these molecules. Instead, the disclosure of the specification is an invitation to the skilled artisan to attempt to discover such a disease that is associated with the instantly claimed nucleic acids, and can thus be detected in a diagnostic which utilizes these nucleic acids. Thus, "real world" disease or illness condition correlation is absent for the claimed subject matter, and the asserted utility of the instant nucleic acids in diagnostic applications is not substantial.

The specification further asserts a number of additional possible utilities for the claimed nucleic acids, including as hybridization probes, as oligomers for PCR, use for chromosome and gene mapping, use in the recombinant production of PANEC-2, and use in the generation of anti-sense DNA or RNA, their chemical analogs, and the like (p. 8, third full paragraph). These utilities are not specific because they can generally be applied to any nucleic acid that encodes a protein, of which there are millions of possibilities. Further, these utilities are not substantial. For example, a nucleic acid may be utilized to obtain a protein. The protein could then be used in conducting research to functionally characterize the protein. The need for such research clearly indicates that the protein and/or its function is not disclosed as to a currently available or substantial utility. A starting material that can only be used to produce a final product does not have substantial asserted utility in those instances where the final product is not supported by a specific and substantial utility. In this case none of the proteins that are to be produced as final products resulting from processes involving claimed nucleic acid have asserted or identified specific and substantial utilities. The research contemplated by applicants to

characterize potential protein products, especially their biological activities, does not constitute a specific and substantial utility. Identifying and studying the properties a protein itself or the mechanisms in which the protein is involved does not define "real world" context or use. Similarly, the other listed and asserted utilities as summarized above or in the instant specification are neither substantial nor specific due to being generic in nature and applicable to a myriad of such compounds.

Neither the specification as filed nor any art of record discloses or suggests any property or activity for the nucleic acid and/or protein compounds such that another non-asserted utility would be well established for the compounds. In the instant specification in the fourth full paragraph on page 4, applicants set forth a research proposal for "new diagnostic techniques" and for "use in the development of effective therapies." This statement in itself appears to be an invitation to conduct further research to reasonably confirm that a specific and substantial utility exists for the claimed molecules. It is noted that a number of examples have been set forth for the basic isolation and characterization of PANEC-2 starting in the instant specification on pages 13-15. From pages 16-26 of the specification a review of generic methods are given with only speculation as to what specific or substantial effects are connected to PANEC-2. These are also clearly research proposals which lack patentable utility. In summary, the instant invention, as filed, has not been set forth with a patentable utility due to a lack of specific, substantial, or well established utility.

Claims 1-10, 12, 13, 60, 61, and 62-65 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and

substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 112-Written Description

8. Claims 3, 4, 6-8, 9, 12, 13, 62, 64, 65, and 66 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Rejected claim 3 is drawn to isolated polynucleotides encoding a polypeptide consisting essentially of an amino acid sequence of SEQ ID NO: 4, or a polypeptide that is a variant of SEQ ID NO: 4, wherein said variant shares at least 90% sequence identity with SEQ ID NO: 4 "has chemokine activity," or a biologically active fragment of a polypeptide consisting essentially of an amino acid sequence SEQ ID NO: 4, wherein said fragment has chemokine activity, or an immunogenic fragment of a polypeptide consisting essentially of an amino acid sequence of SEQ ID NO: 4, wherein the fragment is capable of generating an antibody that specifically binds to the polypeptide of SEQ ID NO: 4, and the immunogenic fragment possesses biological activity.

The subject matter of part (a) is adequately described.

The subject matter of part (b) includes nucleic acids that encode variants of SEQ ID NO: 4 which are not described in the specification, including nucleic acids which encode molecules from other species of related animals, allelic variants, splice variants and the like. Further, the claims do not recite a requisite structure/function relationship between a recited function in the claims and a function of the encoded amino acid. Though the claim recites that the encoded

variant must have "chemokine activity" this recitation of function is very broad, as chemokines are known to be active in a variety of ways, as proteins that bind to receptors that then transmit a wide variety of possible signals within a cell. There is no clear relationship between the structure recited in part (b) of the claim and the recited "function."

Considering part (c) the polynucleotide of claim 3, this genus of nucleic acids is also quite broad, because while the claim requires that the encoded fragment be "biologically active" and have "chemokine activity" this could include any number of possible amino acid residues. Since these two recited functions are broad in their nature (biological activity encompassing even an activity such as being a substrate for a protease or the ability to raise an antibody), these functions do not help to define the claimed genus. Furthermore, the specification does not discuss which fragments of SEQ ID NO: 4 are essential for the maintenance of "chemokine activity" a fact that is particularly relevant in view of the fact that the specification does not even demonstrate what type of chemokine activity SEQ ID NO: 4 possesses to begin with. Furthermore, the claim is open in nature, requiring only that the claimed polynucleotide encode a fragment of SEQ ID NO: 4 that meets the functional language of the claim, but that polynucleotide could further encode other fragments flanking the fragment of SEQ ID NO: 4, and so the claimed polynucleotide encompasses polynucleotides that encode related chemokines, allelic variants not disclosed, as well as possible splice variants of the disclosed nucleic acid.

Part (d) of claim 3 encompasses any nucleic acid encoding any immunogenically active fragment of SEQ ID NO: 4 wherein the fragment is "capable" of generating an antibody that "specifically binds" to SEQ ID NO: 4. The specification at page 12 teaches that antibodies inherently specifically bind their target as opposed to other target sequences, and so in this case,

the language "specifically binds" is quite broad in nature and does not provide a defining characteristic, as any antibody raised by a fragment of SEQ ID NO: 4 would specifically bind some portion of SEQ ID NO: 4. Furthermore, the claim is open in nature, requiring only that the claimed polynucleotide encode a fragment of SEQ ID NO: 4 that meets the functional language of the claim, but that polynucleotide could further encode other fragments flanking the fragment of SEQ ID NO: 4, and so the claimed polynucleotide encompasses polynucleotides that encode related chemokines, even polypeptides that are not chemokines but share some amino acid sequence in common with SEQ ID NO: 4, allelic variants not disclosed, as well as possible splice variants of the disclosed nucleic acid.The genus of nucleic acids encompassed within this claim includes a wide variety of polynucleotides encoding amino acid sequences that are not described.

Claim 4 encompasses any polynucleotide which encodes a polypeptide "of" SEQ ID NO: 4, which includes any polynucleotide that encodes any portion of SEQ ID NO: 4 (polypeptide "of" requires encoding only minimally two amino acids) within any larger context, and thus encompasses many, many hundreds of thousands of molecules.

Claims 6-8 are drawn to constructs and methods that utilize or comprise nucleic acids of claim 3.

Claim 9 depends from claim 1 and encompasses all of the subject matter previously discussed with regard to claim 3. Further, claim 9 encompasses nucleic acids which encode polypeptides as recited in part (b) of claim 1. Part (b)(iii) of claim 1 recites that the encoded variant has an insertion of 1-5 amino acids as compared to SEQ ID NO: 4. This recitation using the word "has" is open claim language, and so, while the language of the claim requires that the variant has 1-5 amino acid inserted or deleted, this requirement is a MINIMUM requirement as

to the number of insertions or deletions permitted within the language of the claim. Furthermore, when this is combined with part (b)(ii) of the claim which requires certain amino acid residues to be present (note parts (iii) and (ii) are linked using and/or) it means that even part (ii) which recites the amino acid residues that must be present in the encoded polypeptide is permitted to have any number of deletions or insertions between the residues. Essentially this combination of permitted changes in the variants recited in claim 3(b) results in very little required structure of the encoded polypeptide relative to SEQ ID NO: 4. Like in claim 3, this claim requires that the encoded polypeptide have "chemokine activity," and like the other claims, this function is not correlative with any particular structure disclosed in the specification.

Claim 12 encompasses any polynucleotide "of" SEQ ID NO: 3, which includes any polynucleotide comprises any portion of SEQ ID NO: 3 (polynucleotide "of" requires minimally only two nucleotides) within any larger context, and thus encompasses many, many hundreds of thousands of molecules.

Claim 13 claims an isolated polynucleotide comprising at lest 60 contiguous nucleotides of a polynucleotide of SEQ ID NO: 3. Claim 13 is drawn using broad "comprising" language, and encompasses polynucleotide fragments of 60 nucleotides with any potential flanking sequences. The claim has no functional requirement. The claim thus encompasses any number of splice or allelic variants of SEQ ID NO: 3, as well as potential genomic sequences any of which encode molecules with any potential function.

Claims 62, and 64-65 are drawn to isolated polynucleotide sequences encoding a polypeptide that comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence of SEQ ID NO: 4 and possessing chemokine activity. The claims

encompass nucleic acids that encode variants of SEQ ID NO: 4 which are not described in the specification, including nucleic acids which encode molecules from other species of related animals, allelic variants, splice variants and the like. Further, the claims do not recite a requisite structure/function relationship between a recited function in the claims and a function of the encoded amino acid. Though the claim recites that the encoded variant must have "chemokine activity" this recitation of function is very broad, as chemokines are known to be active in a variety of ways, as proteins that bind to receptors that then transmit a wide variety of possible signals within a cell. There is no clear relationship between the structure recited in part (b) of the claim and the recited "function."

Claim 66 recites an isolated polynucleotide that encodes a "polypeptide variant" wherein the variant has conservative amino acid substitutions and possesses chemokine activity. The claim is entirely devoid of any structural limitation as it does not provide any reference sequence against which the "substitutions" are compared, and thus, encompasses any molecule discovered or undiscovered that has any potential "chemokine" activity.

Within the genus of the claimed polynucleotides, the instant specification describes only nucleic acids encoding SEQ ID NO: 4, with a particular example of a nucleic acid comprising instant SEQ ID NO: 3. Molecules that consist of fragments of SEQ ID NO: 3 are also described, as are molecules that encode amino acids sequences consisting of fragments of SEQ ID NO: 4. As discussed, however, the claims encompass any number of variants and sequences related to SEQ ID NO: 3 and encoding polypeptides related to SEQ ID NO: 4 that are not described in the specification. It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that

> "...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved

> until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

In the instant application, only the nucleic sequence of the disclosed SEQ ID NO: 3 and encoding SEQ ID NO: 4 are described. Also, in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

> "...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

In the application at the time of filing, there is no record or description which would demonstrate conception of any nucleic acids encoding proteins modified by addition, insertion, deletion, substitution or inversion with the disclosed SEQ ID No: 4 therefore possessing one or more amino acid differences such that a different amino acid sequence is encoded which retains same function as SEQ ID NO: 4, which function is not clearly set forth in the specification.

Claim Rejections - 35 USC § 112, 2nd Paragraph

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 3, 6, 7, 8, 9, 10, 12, 60, 61, 64, 65, and 66 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 is indefinite over the recitation in part (a) of the claim "consisting essentially of **an amino acid** sequence of SEQ ID NO: 4" because it is not clear if "an amino acid sequence of SEQ ID NO: 4" means a sequence selected from within SEQ ID NO: 4 or if it requires the

presence of SEQ ID NO: 4 in its entirety. Claims 6-8 depend from claim 3 and are also indefinite over this recitation.

Claim 3 is indefinite over the recitation in part (b)"the variant shares at least 90% sequence identity with SEQ ID NO: 4 has chemokine activity" because it is not clear if the phrase "has chemokine activity" is meant to modify SEQ ID NO: 4 or the variant. Claims 6-8 depend from claim 3 and are also indefinite over this recitation.

In part (c) of claim 3, the recitation "a biologically active fragment of a polypeptide consisting essentially of an amino acid sequence of SEQ ID NO: 4" is indefinite because it is not clear if the "consisting essentially of" phrases is meant to modify the "biologically active fragment" or "of a polypeptide" portion of the claim. Claims 6-8 depend from claim 3 and are also indefinite over this recitation.

In part (d) of claim 3, the recitation "an immunogenic fragment of a polypeptide consisting essentially of an amino acid sequence of SEQ ID NO: 4" is indefinite because it is not clear if the "consisting essentially of" phrases is meant to modify the "immunogenic fragment" or "of a polypeptide" portion of the claim. Claims 6-8 depend from claim 3 and are also indefinite over this recitation.

Claim 4 is indefinite over the recitation "a polypeptide **of** SEQ ID NO: 4" because it is not clear if a polypeptide of SEQ ID NO: 4 is any polypeptide from within SEQ ID NO: 4 (and therefore is "of" SEQ ID NO: 4) or if SEQ ID NO: 4 in its entirety is required.

Claims 9 and 10 depends from claim 1 which recites in part (a) "a polypeptide comprising **an** amino acid sequence of SEQ ID NO: 4" which is indefinite because it is not clear

if "an amino acid sequence of SEQ ID NO: 4" means a sequence selected from within SEQ ID NO: 4 or if it requires the presence of SEQ ID NO: 4 in its entirety.

Claims 9 and 10 depends from claim 1 which recites in part (b) "a polypeptide encoding an allelic or recombinant variant." This language is indefinite because it is not clear what is meant by the recitation that the polypeptide encode a variant, as polypeptides are not generally considered to encode other molecules, but instead themselves are encoded by polynucleotides. Clarification is required.

Claim 12 is indefinite over the recitation comprising "**a** polynucleotide sequence of SEQ ID NO: 3" in part (a) and "encodes **an** amino acid sequence of SEQ ID NO: 4" in part (b) because it is not clear if this language is meant to include only a sequence from within SEQ ID NO: 3 or SEQ ID NO: 4 or SEQ ID NO: 3 and SEQ ID NO: 4 in their entirety. Likewise, parts (c) and (d) recite "a polynucleotide of a): and "a polynucleotide of b)" and it is not clear if these refer back to the entire polynucleotides recited in parts (a) and (b) or if they also encompass only a sequence of these polynucleotides, that is a sequence from within them. Claims 60 and 61 are indefinite because they depend from claim 12.

Claims 64 and 66 are indefinite because they recite "having one or more conservative amino acid substitution(s)" but they do not recite a reference sequence with which the substitutions are relative to, and therefore it is indefinite as to how to determine if the substitutions are present.

Claim 65 is indefinite over the recitation "a polypeptide that consists essentially of an insertion or deletion of about 1 to 5 amino acids" because it is not clear what it means for a polypeptide to consist of an insertion or a deletion. For example, does consists essentially of an

insertion of 5 amino acids mean that the claimed polynucleotide encode a 5 amino acid polypeptide that would have been deleted from SEQ ID NO: 4?

Claim Objections

11. Claims 12 is objected to because the claim does not end with a period. MPEP 608.01(m) states, "Each claim begins with a capital letter and ends with a period. Periods may not be used elsewhere in the claims except for abbreviations." Claim 12 is further objected to because the reference characters "c," "d," and "e" are not enclosed with parentheses to avoid confusion with the rest of the claim. The MPEP also at 608.01(m) states that reference characters "should be enclosed within parentheses so as to avoid confusion with other numbers or characters which may appear in the claims. The use of reference characters is to be considered as having no effect on the scope of the claims."

12. Claim 66 is objected to over the recitation "one or more conservative amino acid substitution" because the word "substitution" should be the plural "substitutions" in order to agree with the "one or more."

Claim Rejections - 35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

14. Claims 3, 4, 6-9, 12, and 66 are rejected under 35 U.S.C. 102(b) as being anticipated by Caput *et al.* (WO 92/09629).

For applicant's convenience it is noted that the PCT application represented by this WO publication matured into a 371 application filed in the United States which issued as US 6001649. This US Patent provides an English language translation of the French PCT relied upon in this rejection.

Caput *et al.* teach an isolated nucleic acid encoding a an immunogenic fragment of a polypeptide having an amino acid sequence of SEQ ID NO: 4 wherein said fragment is capable of generating an antibody that specifically binds to the polypeptide of SEQ ID NO: 4. Caput *et al.* teach a polynucleotide that encodes residues 75-78 of SEQ ID NO: 4, and this four amino acid fragment would be immunogenically active, that is able to raise an antibody. The raised antibody would specifically bind to this portion of SEQ ID NO: 4. The specification at page 12 teaches that antibodies inherently specifically bind their target as opposed to other target sequences, and so in this case, the language "specifically binds" is quite broad in nature and essentially applies to any antibody that would bind a target sequence, as any antibody raised by a fragment of SEQ ID NO: 4 would specifically bind some portion of SEQ ID NO: 4. Further, this fragment possesses biological activity insofar as it can raise an antibody, be bound by an antibody or be the substrate for a protease. Thus, the nucleic acid taught by Caput *et al.* meets at least the limitations of claim 3 as recited in part (d).

Caput *et al.* teach an isolated nucleic acid encoding a chemokine.

With regard to claim 4, the isolated polynucleotide taught by Caput *et al.* encodes "a polypeptide" of SEQ ID NO: 4 wherein this language is interpreted to mean a polypeptide of (or from within) SEQ ID NO: 4.

With regard to claim 6, Caput *et al.* teach recombinant polynucleotides comprising a promoter sequence operably linked to their SEQ ID NO: 15 and, with regard to claims 7 and 8, they teach host cells which are transgenic organisms comprising the recombinant polynucleotides.

Claim 9 depends from claim 1 which also encompasses a polynucleotide encoding an immunogenic fragment of SEQ ID NO: 4. With regard to claim 9, Caput *et al.* teach a method for producing the polypeptide encoded by their SEQ ID NO: 15, which comprises culturing a cell under conditions suitable for the expression of the polypeptide, and recovering the polypeptide (Sections 5-7, pages 31-44).

Further, with regard to claim 9, Caput *et al.* teach an isolated polynucleotide encoding a polypeptide that is a polypeptide that is an allelic variant or recombinant variant of the amino acid sequence SEQ ID NO: 4, wherein said variant has an insertion or deletion of 1-5 amino acids as compared to SEQ ID NO: 4 and further wherein the variant has chemokine activity (as also recited in claim 1). The language of the instant claim is drawn using open claim language "has" and thus is interpreted to mean that the claim is meant to encompass any isolated nucleic acid encoding a polypeptide that is a variant of SEQ ID NO: 4 wherein said variant has an insertion or deletion of 1-5 amino acids relative to SEQ ID NO: 4, but can have any number of such insertions or deletions.

The nucleic acid taught by Caput *et al.* encodes a chemokine that has an insertion of three amino acids between residues 27 and 28 of instant SEQ ID NO: 4 (see alignment below, Qy=SEQ ID NO: 4, Db= SEQ ID NO: 15 of Caput *et al.*), thus, the molecule "has" an insertion of three amino acids compared to SEQ ID NO: 4. It is noted that the molecule also contains a

large number of additional insertions and deletions relative to SEQ ID NO: 4, for example, between the first and fourth amino acid residues of SEQ ID NO: 4 there is a deletion of the residues AlaGln and an insertion of residues LysAla. Alternately, this difference could be described as an insertion of a Lys after the first residue of SEQ ID NO: 4, and a deletion of Gln from the third residue of SEQ ID NO: 4. As the claim places no structural limits on the number of insertions or deletions permissible within the scope of the claim, and as the molecule encoded by the polynucleotide taught by Caput *et al.* encodes a cytokine, the reference is considered to teach the invention of claim 9.

With regard to claim 12, the nucleic acid taught by Caput *et al.* encodes "a polynucleotide sequence "of" SEQ ID NO: 3 wherein this limitation is interpreted to mean a sequence from within SEQ ID NO: 3.

With regard to claim 66, the polynucleotide taught by Caput *et al.* is a sequence encoding a variant which has many conservative amino acid substitutions as well as other substitutions and possesses chemokine activity. The claim does not set forth any structural limitations for the claimed polynucleotide, only requiring that it is a "variant" with chemokine activity. All molecules with chemokine activity are variants of one another and all have some conservative and some non-conservative substitutions when compared with one another.

Thus, the teachings provided by Caput *et al.* meet all of the limitations of the rejected claims.

```
Qy          1 MetAlaGlnSerLeuAlaLeuSerLeuLeuIleLeuValLeuAlaPheGlyIleProArg 20
              |||       |||    ||||||       |||:::|||       |||          |||:::
Db         71 ATGAAAGCCTCTGCAGCACTTCTGTGTCTGCTGCTCACAGCAGCTGCTTTCAGCCCCCAG 130

Qy         21 ThrGlnGlySerAspGlyGly---------AlaGlnAspCysCysLeuLysTyrSerGln 37
                              |||          :::       ||||||    ::::::
Db        131 GGGCTTGCTCAGCCAGTTGGGATTAATACTTCAACTACCTGCTGCTACAGATTTATCAAT 190
```

```
Qy         38 ArgLysIleProAlaLysValValArgSerTyrArgLysGlnGluProSerLeuGlyCys 57
              :::||||||||||   :::   :::   ||||||||||:::         |||      |||
Db        191 AAGAAAATCCCTAAGCAGAGGCTGGAGAGCTACAGAAGGACCACCAGTAGC---CACTGT 247

Qy         58 SerIleProAlaIleLeuPheLeuProArgLysArgSerGlnAlaGluLeuCysAlaAsp 77
                    |||:::::::|||      :::   :::         |||:::|||||||||
Db        248 CCCCGGGAAGCTGTAATCTTC------AAGACCAAACTGGACAAGGAGATCTGTGCTGAC 301

Qy         78 ProLysGluLeuTrpValGlnGlnLeuMetGlnHisLeuAsp---LysThrProSerPro 96
              |||   :::   |||||||||      |||:::|||||||||   ||||||   :::|||
Db        302 CCCACACAGAAGTGGGTCCAGGACTTTATGAAGCACCTGGACAAGAAAACCCAAACTCCA 361

Qy         97 Gln 97
              :::
Db        362 AAG 364
```

Claim Rejections - 35 USC § 102

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

16. Claims 3, 4, 5, 6, 7, 8, 9, 10, 62, 63, 64, and 65 are rejected under 35 U.S.C. 102(b) as being anticipated by Hromas *et al.* (J. Immunol 159(6)2554-2558 (1997)), as evidenced by GenBank Accession number U88320 (18 December 1997).

Hromas *et al.* is available as prior art for this rejection because the rejected claims are not entitled to priority under 120 to the parent application because they all include subject matter that is not supported by the specification of the parent application (see heading "Priority" in this office action).

Hromas *et al.* teach the isolation of a cDNA sequence containing the entire open reading frame of a molecule referred to therein as human Exodus-2 (p. 2554, 2nd column, heading

"Isolation"). Hromas *et al.* teach that the sequence was submitted to GenBank as accession U88320. Nucleotides 15-416 of this molecule encode instant SEQ ID NO: 4.

Therefore, with regard to claim 3, Hromas *et al.* teach an isolated polynucleotide encoding a polypeptide consisting essentially of the amino acid sequence of SEQ ID NO: 4.

With regard to claims 6, 7, and 8, Hromas *et al.* teach that the complete cDNA was cloned into an expression vector and isolation of the protein from sF9 cells. With regard to claims 9 and 10, Hromas *et al.* teach culturing the cell to express the polypeptide and recovering the polypeptide(p. 2555, 1st column, Recombinant Exodus-2 production).

With regard to claim 62, Hromas *et al.* teach an isolated polynucleotide encoding a polypeptide that comprises an amino acid sequence having at least 90% sequence identity to the amino acid sequence of SEQ ID NO: 4 and possesses chemokine activity.

With regard to claim 63, the polynucleotide encodes a polypeptide consisting essentially of SEQ ID NO: 4.

With regard to claim 64, the polynucleotide encodes a polypeptide having one or more conservative amino acid substitutions. The reference is applied to this claim because the claim does not set forth a reference sequence that the substitutions are relative to, and relative to some arbitrary chemokine sequence there are any number of conservative amino acid substitutions, depending on the sequence.

With regard to claim 65, the polynucleotide encodes a polypeptide that has zero deletions compared with SEQ ID NO: 4. The claim is indefinite but this rejection is written against a claim that requires about 1 to 5 amino acid deletions compared with SEQ ID NO: 4. Hromas *et al.* teach a polynucleotide encoding a polypeptide having zero deletions, which is "about 1."

Therefore, the teachings of Hromas *et al.* anticipate each of the rejected claims.

Response to Remarks

New grounds of rejection are set forth.

The objections to the specification are withdrawn in view of the amendments to the specification.

The new matter rejection set forth with regard to the language in claim 1 is maintained for claims 9 and 10 because these claims remain dependent from claim 1 and claim 1 was not amended. The rejection is applied to newly added claim 65 which recites the limitation of "an insertion or deletion of about 1 to 5 amino acids compared with SEQ ID NO: 4."

The rejection of claims 60 and 61 for new matter with regard to the "non-genomic" and "without introns" limitations are maintained because applicant did not amend these claims or set forth arguments to traverse the rejections.

The **written description rejection** is maintained and applied to the newly added claims. It is also newly applied to claims 4 and 12 in view of the indefinite nature of the claim language which requires sequence "of" particular SEQ ID NO.

Applicant traverses the rejection. Applicant argues that because of the redundancy in the genetic code and the teachings of the instant application, a skilled artisan would know what amino acids can be changed within SEQ ID NO: 4 in order to produce a "functionally equivalent protein (p. 11, 1st ¶)." This is not persuasive, since the function of SEQ ID NO: 4 is not taught in the specification. The specification asserts that SEQ ID NO: 4 has "chemokine activity," which is a broad statement of functionality that varies among even members of this class of proteins, as discussed in the rejection. There is no identification of a particular structure in the specification

that is correlative with this function. The specification teaches at example XII how to screen for various different potential chemo attractant activities, but not which ones are possessed by SEQ ID NO: 4. Applicant is in possession of a molecules (SEQ ID NO: 4) and nucleic acids encoding that molecule which certainly possess a particular activity, but applicants have not disclosed what this activity is.

Applicant further argues that "the function of chemokines is well known in the art, as is also explained in the instant specification. See specification at 3. (p. 11, section (2)). The specification discusses generally a number of activities of chemokines, and regarding C-C chemokines, the specification teaches that "relatively few have been described" and then follows with "a brief description" of the known C-C chemokines. The specification does not teach the activity of any of these.

As discussed in the utility rejection herein, chemokines are chemoattractant cytokines. In a 1994 review of chemokines, Schall *et al.* teach that "Although the properties of these molecules have only recently begun to be elucidated, the bulk of the evidence to date suggests that the chemokines function as regulators of inflammatory and immunoregulatory processes, particularly through their leukocyte chemoattractant effects (p. 4, third paragraph, as cited in the IDS)." A "leukocyte" is a white blood cell, and includes among its members monocytes, neutrophils, basophils, eosinophils, and lymphocytes, each of which function differently within the body's immune system. Furthermore, Schall *et al.* provide a table which summarizes different sources and targets for the known C-C type chemokines (Table V). Some of these, for example MCP-1, can be isolated from many tissues, while others can be isolate from only T cells (for example I-309). Likewise, with regard to targets, some of the C-C type chemokines target a

wide variety of cells, for example MIP-1α targets a variety of leukocytes as well as stem cells, osteoclasts, and hypothalamus. And for some the target is yet unknown, such as the murine C-C chemokine C10. Furthermore, Schall *et al.* teach that even chemokines with a great deal of structural homology (70%) demonstrate distinct specificities for their cellular targets (p. 16, first full paragraph), and that attempts to even elucidate the targets of chemokines contain "pitfalls of interpretation (p. 23, second paragraph)." The pancreas is a complex organ with many cell types- the specification does not provide any information as to what type of cells produce or are targeted by PANEC-2. Thus, in the instant case, while applicant may have identified a C-C type chemokine, this designation does not speak specifically to the functioning of the molecule with regard to target, and further experimentation (which is unpredictable) would be required to determine such a target.

Applicant states at the top of p. 12 of the response that "the Examiner's assertion that the 'function [of SEQ ID NO: 4] is not clearly set forth in the specification" is incorrect." However, applicant does not point to any portion of the specification that clearly sets forth the function of SEQ ID NO: 4. Applicant only points to portions of the specification that discuss a variety of functions that are assigned to different chemokines. The specification does not teach the target nor the specificity of the SEQ ID NO: 4.

Applicant argues at page 12, section 3, that one could asses the immunogenic or biological activity of fragments of SEQ ID NO: 4. The written description rejection is set forth against these claims insofar as they are not limited to isolated nucleic acids consisting of polynucleotide that encode amino acids consisting of fragments of SEQ ID NO: 4, but instead

include flanking sequences which are not described and lead to the claim encompassing any number of variants as well as genomic sequences, etc.

The discussion of "naturally occurring (p. 12 (4))" sequences is moot in view of the cancellation of this language from the claims.

Therefore, even in view of applicant's remarks, the rejection is MAINTAINED.

The **112 2nd rejection** of claims 9 and 10 is maintained because these claims remain dependent upon claim 1 which has not been amended. Applicant's arguments do not address the fact that it is not clear how a polypeptide encodes an allelic or recombinant variant. The issue at the hear of the 112 2nd rejection is that the claim recites that the **polypeptide encodes** when polypeptides do not encode molecules, they themselves are encoded by nucleic acids.

The rejection for **lack of utility** is maintained. Applicants point out that the specification asserts that the claimed polynucleotides encode polypeptides that are members of the C-C chemokine family and "are useful in diagnostic assays based on chemokine production in cases of inflammation or disease affecting the pancreas (see remarks, p. 14, 1st ¶). The asserted utility of the claimed PANEC-2 encoding nucleic acids as a tool in diagnostics is not substantial because the specification does not teach or suggest the "inflammatory or disease" affecting the pancreas that can be identified using these molecules. Instead, the disclosure of the specification is an invitation to the skilled artisan to attempt to discover such a disease that is associated with the instantly claimed nucleic acids, and can thus be detected in a diagnostic which utilizes these nucleic acids. Thus, "real world" disease or illness condition correlation is absent for the claimed subject matter, and the asserted utility of the instant nucleic acids in diagnostic applications is not substantial.

Likewise, applicants assert that the encoded chemokines can be used to make antibodies that can be used to treat disease or inflammation. Again, this is not a substantial utility for the claimed invention because no such disease or condition that can be treated with these antibodies has been identified. This is merely an invitation to conduct further experimentation to reasonably confirm if any disease treatment is possible, and if so, which diseases.

Applicants argue that the molecules "can lead to activation of cells such as monocytes, macrophages and T-lymphochtes" and so assay for PANEC allows for accelerated diagnosis and proper treatment of tissue damage or destruction that could be caused by such activation. Again, this is not a substantial utility for the claimed invention because applicant has not demonstrated which molecules are activated (if any are), under what conditions, or that such activation does lead to a condition that can be diagnosed based on PANEC-2 overexpression.

Applicants point out that they are not required to disclose a mechanism or target cell population by which the PANEC polypeptides work. This is not being required. The examiner is only requiring the assertion of a specific, substantial, and credible utility, and for the reasons of record as set forth in these arguments and in the rejection of record, the rejection is MAINTAINED.

With regard to the **102(b)** rejection, the rejection is MAINTAINED. At the top of page 16 applicant argues that the immunogenic fragment of SEQ ID NO: 4 encoded by the molecule taught by Caput does not also posses biological activity. As discussed in the rejection, "biological activity" as broadly interpreted includes the ability to raise antibodies or be a substrate for a protease, both of which the fragment taught by Caput *et al.* posses. Therefore the rejection is maintained.

The previously set forth claim objections are withdrawn.

The application is in compliance with the sequence rules.

Conclusion

17. No claims are allowed.

18. Claim 5 and 10 are free of the prior art. The prior art does not teach or suggest an isolated polynucleotide encoding SEQ ID NO: 4, and in particular does not teach an isolated polynucleotide comprising instant SEQ ID NO: 3.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C Switzer whose telephone number is (571) 272-0753. The examiner can normally be reached on Monday through Friday, from 9:00 AM until 4:00 PM.

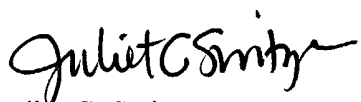
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached by calling (571) 272-0782.

The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571)272-0507.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of

the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.



Juliet C. Switzer
Examiner
Art Unit 1634

September 10, 2004